Remarks

Claims 1, 4, 7, 10, 13, 16, 19, 20, 21, 23, 28-30, 34-38, and 64-131 will be pending in the instant application on entry of the present amendment. Claims 33, 40, 44 and 46, which have been withdrawn from consideration by the Examiner as being directed to nonelected subject matter, have been cancelled without prejudice or disclaimer. Applicants reserve the right to pursue claims to the cancelled subject matter in one or more divisional applications. Claims 1, 20, 21 and 23 have been amended in order to restrict the claims to previously elected subject matter of the present invention. Claim 1 has been further amended to recite "encoded by the cDNA clone contained in ATCC Deposit No. PTA-507." Claim 21 has been further amended to recite "of at least 9 amino acids," support for this amendment may be found in the specification as filed at paragraph number [0266]. Further support for amendment of claims may be found throughout the specification as originally filed. Accordingly, no new matter has been added by amendment.

I. Information Disclosure Statement

The Examiner has advised that "reference AB in the IDS filed Dec. 11, 2001 appears to be the incorrect reference, since there is no inventor named Rosen and there are no sequences in the published application 20030058697." See, Paper No. 8, page 7. Applicants respectfully point out that no IDS was filed December 11, 2001 in connection with the present application, which was itself not filed with the U.S.P.T.O. until January 16, 2002. However, an IDS was filed on February 10, 2003, which listed Rosen et al. Application No. 09/912,293 (unpublished) as reference AB. Applicants provided a copy of relevant portions of Rosen et al. with the IDS filed February 10, 2003. The Examiner is

requested to telephone the undersigned if a copy of the reference is not present in Office files.

II. Specification

The specification has been amended to address the informalities identified and objected to by the Examiner. *See*, Paper No. 8, pages 7-8. The title of the invention has been amended as suggested by the Examiner in Paper. No. 8. The Brief Description of the Figures has been amended to recite "Figures 1A-D", "Figures 2A-D", "Figures 4A-E", "Figures 7A-E" and "Figures 8A-D," and this amendment has been further incorporated wherever these figures are recited throughout the specification. On page 94, line 14 the definition of the TR13 transmembrane domain has been amended to recite "amino acid positions from about 907 to about 931," the amendment is in accordance with the description of the extracellular domain as found in the "Brief Description of the Figures" at paragraph **[0039]**. On page 94, lines 17-19 the definition of the TR13 extracellular domain has been amended to recite "amino acid positions from about 42 to about 906," the amendment merely corrects a typographical error which had resulted in the recitation of "42 to about 96" and is in accordance with the description of the extracellular domain as found in the "Brief Description of the Figures" at paragraph **[0039]**. Support for these amendments to the specification may be found throughout the specification and drawings as originally filed. Accordingly, no new matter has been added by amendment.

III. Rejections under 35 U.S.C. § 112, first paragraph

A. Enablement

The Examiner has rejected claims 1, 13, 16, 19 and 104-131, under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement since "[t]he claims contain subject matter which was not described in the specification in such a way as to enable one of skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." *See*, Paper No.8, pages 8-9. Applicants respectfully disagree and traverse the rejection.

In rejecting claims 1, 13, 16, 19 and 104-131, under 35 U.S.C. § 112, first paragraph, the Examiner asserts that "Applicants referral to the deposit of PTA-507 (HWLHN83) on page 5 of the specification is an insufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have been met." Applicants respectfully direct the Examiner's attention to the enclosed Statement Concerning the Deposited cDNA.

In view of the enclosed Statement Concerning the Deposited cDNA, Applicants believe the Examiner's concerns have been fully addressed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection, under 35 U.S.C. § 112, first paragraph, for lack of enablement.

B. Written Description

The Examiner has further rejected claims 1, 20, 21, 23, 28-30, 34-38, 64, 65, 68, 71, 74-77, 80, 83, 86-105, 107, 109, 111, 113, 115 and 117-130, under 35 U.S.C. § 112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention." *See*, Paper No. 8, page 9.

The Examiner further alleges that "the claims as written include polypeptides comprising fragments and homologues, encompass polypeptides that vary substantially in length and also in amino acid composition." *See*, Paper No. 8, page 9, lines 12-13. The rejection is respectfully traversed. Applicants assert that each of the claims pending prior to and after the present amendment is fully supported and satisfies the statutory written description requirements under 35 U.S.C. § 112.

In an analysis of written description under 35 U.S.C. § 112, first paragraph, the Examiner bears the initial burden of presenting a *prima facie* case of unpatentability. This burden is only discharged if the Examiner can present evidence or reasons why one skilled in the art would not reasonably conclude that Applicants possessed the subject matter as of the priority date of the present application. *In re Wertheim*, 541 F.2d 257, 262, 191 U.S.P.Q.2d 90, 96 (C.C.P.A. 1976); M.P.E.P. § 2163.04. In the instant case, Applicants maintain that the Examiner has not met this burden.

Claims 1, 20, 21, 23, 28-30, 34-38, 64, 65, 68, 71, 74-77, 80, 83, 86-105, 107, 109, 111, 113, 115 and 117-130, stand rejected because polypeptides encoded by polynucleotides encompassed by the present claims are alleged not to be functionally or structurally described beyond the encoded polypeptide sequence or the polynucleotide sequence that encodes that polypeptide. The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor had possession of the claimed invention based on the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02. Indeed, as the Federal Circuit has noted, "the issue is whether one of skill in the art could

derive the claimed ranges from the patent's disclosure." *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d 989, 54 U.S.P.Q. 2d 1227 (Fed. Cir. 2000) (emphasis added).

It is well established that a "gene is a chemical compound, albeit a complex one". *Amgen, Inc. v. Chugai Pharamceutical Co., LTD.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). Thus, the claims of the instant application, directed to particular polynucleotides encoding polypeptides having the amino acid sequences of SEQ ID NO:39 or encoded by ATCC Deposit No. PTA-507, are essentially chemical claims involving generic chemical formulae. As stated by Judge Lourie in *University of California v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997), "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass." All of the objectives met by a generic chemical formula are similarly met by the explicit description in the instant specification of a polynucleotide sequence (*i.e.* SEQ ID NO:39), the amino acid sequence encoded thereby (SEQ ID NO:40), and by the instant claims to polynucleotides at least 95% identical to polynucleotides encoding polypeptides comprising amino acid sequences of SEQ ID NO:40, and polynucleotides encoding polypeptides comprising amino acid sequences at least 95% identical to amino acid sequences of SEQ ID NO:40. That is, the instant claims clearly distinguish the boundaries of the claimed genera and identify all of the members of those genera. Accordingly, one skilled in the art would reasonably conclude that Applicants had possession of the polypeptides encompassed by the rejected claims upon reading the present application as filed, and would immediately recognize that the Applicants had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563). Therefore, the specification contains an adequate

written description of the claimed polypeptides. Applicants have provided the skilled artisan with a "generic formula" in the form of the amino acid sequence of SEQ ID NO:40, which indicates "with specificity what the generic claims encompass." Armed with this information "one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass."

Furthermore, the specification particularly teaches on embodiments of the invention rejected by the Examiner in the present action. Accordingly, one skilled in the art, enlightened by the teachings of the present application, could readily envision all of the various polynucleotide sequences that comprise the specified polynucleotides. For example, the skilled artisan could easily substitute a nucleic acid codon encoding any given amino acid residue for a codon encoding any other given residue, or add or delete codons, such that nothing more than what is described in the specification would be required to identify every single one of the polynucleotides at least 95% identical to polynucleotides encoding polypeptides comprising amino acid sequences of SEQ ID NO:40, or polynucleotides encoding polypeptides comprising amino acid sequences that are at least 95% identical to the amino acid sequence of SEQ ID NO:40. Thus, it would be readily apparent to the skilled artisan that the Applicants had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563).

For all of the above reasons, Applicants respectfully assert that the Examiner has failed to meet the required burden in presenting evidence or reasons why those skilled in the art would not recognize the claimed invention from the disclosure. Moreover, the specification conveys with reasonable clarity that Applicants were in possession of the claimed invention. Therefore, Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully

request that the Examiner's rejection of the claims under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

The Examiner has concluded that "[g]iven the unpredictability of homology comparisons, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim." *See*, Paper No. 8, page 11, lines 1-4. However, the burden is on the Examiner to establish that a representative number of species have not been disclosed to support of the genus claim. It is clear that the Examiner has failed to meet this burden or provide any showing that one skilled in the art would not reasonably conclude that Applicants possessed the claimed subject matter as of the priority date of the present application. Applicants respectfully submit that the entire claimed genus of polypeptides is described such that a skilled artisan would recognize that Applicants were in possession of the genus. Applicants have not only described the single species having the sequence of SEQ ID NO:39, which encodes the entire amino acid sequence of SEQ ID NO:40, they have also provided a description sufficient to allow the skilled artisan to readily envision the additions, deletions, and substitutions falling within the claims. The claims recite polynucleotides that encode polypeptide molecules which comprise portions of the amino acid sequence of SEQ ID NO:40 with some variants as directed by the specification. The claims therefore read on described polynucleotide sequences. Accordingly, the Examiner's rejection under 35 U.S.C. § 112, first paragraph, for lack of adequate description should be withdrawn.

Accordingly, Applicants respectfully request that the present rejection under 35 U.S.C. § 112, first paragraph, for lack of adequate written description, be reconsidered and withdrawn.

IV. Rejections under 35 U.S.C. § 112, second paragraph

The Examiner has further rejected claims 1, 4, 7, 10, 13, 16, 19-21, 23, 28, 30 and 34-38 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite "because claim 1 recites a nucleotide sequence encoding **the** TR13 extracellular or intracellular domain, and there are two TR13 proteins disclosed that have different extracellular and intracellular domains." *See*, Paper No.8, page 12 (emphasis in original).

Applicants respectfully disagree and traverse the rejection. However, in the interest of expediting prosecution, Applicants have amended claim 1 to recite "encoded by the cDNA clone contained in ATCC Deposit No. PTA-507" thereby mooting the present rejection.

Accordingly, Applicants respectfully request that the present rejection, under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

V. Priority

The Examiner has denied the claim of the present application to the benefit of prior application 09/618,570 and prior provisional applications under 35 U.S.C. §§120 and 119(e) respectively. *See*, Paper No. 8, pages 12-13. Accordingly, the Examiner has awarded an effective priority date of January 16, 2002, to the present application allegedly "because the parent applications were not supported by either a specific and substantial utility or a well established utility." *See*, Paper No. 8., page 13. Applicants respectfully disagree and traverse this determination.

Determination that an application is not supported by either a specific and substantial utility or a well established utility, analogous to a rejection under 35 U.S.C. §

101, is improper when a person of ordinary skill in the art would find credible disclosed features or characteristics of the invention, or statements made by the applicant in the written description of the invention. *See,* M.P.E.P. §§ 2107.02(II), (III) at 2100-[38-40] (Feb. 2003). In addition, an applicant need only make *one* credible assertion of utility for the claimed invention to satisfy 35 U.S.C. § 101. *See, e.g., Raytheon v. Roper,* 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983), *cert. denied,* 469 U.S. 835 (1984) ("When a properly claimed invention meets at least one stated objective, utility under 35 U.S.C. § 101 is clearly shown."). *See,* M.P.E.P. at 2100-37. Finding a lack of utility is also improper if a person of ordinary skill in the art would know of a use for the claimed invention at the time the application was filed. *See,* M.P.E.P. § 2107.02(II)(B) at 2100-[38-39]. Moreover, the burden is on the Examiner to establish why it is more likely than not that one of ordinary skill in the art would doubt *(i.e.,* "question") the truth of the statement of utility. *See,* M.P.E.P. § 2107.02(III) at 2100-[39-40] (emphasis added). Thus, the Examiner must provide evidence sufficient to show that the statement of asserted utility would be considered "false" by a person of ordinary skill in the art. *Id.* The Examiner must also present countervailing facts and reasoning sufficient to establish that a person of ordinary skill would not believe the applicants' assertion of utility. *See id.*; *see also, In re Brana,* 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). For the reasons set forth below, the Examiner has not met the burden that is necessary to establish and maintain a determination that none of the presently claimed priority applications are supported by either a specific and substantial utility or a well established utility for lack of utility under 35 U.S.C. § 101.

Applicants point out that the Examiner's assertion that "[a]pplicants for the first time have supplied a specific and substantial utility, that of binding Fas Ligand, which was

not contemplated or disclosed in the parent application" is improperly based. *See*, Paper No. 8, page 12. Contrary to the Examiner's comments, Applicants have set forth in the earliest provisional application to which the present application claims priority benefit, statements that clearly and fully describe the function of TR13 of the present invention and explain why Applicants believe the invention is useful.

The earliest provisional application to which the present application claims priority benefit under 35 U.S.C. § 119(e) is Provisional application No. 60/144,087, filed July 16, 1999 (the '087 application). The '087 application teaches that TR13 is a novel member of the Tumor Necrosis Factor Receptor family of polypeptides, that it is involved in the regulation of apoptosis, and that it is expressed in a number of tissue and cell types and specifically that it is found in resting and activated T-cells as well as apoptotic T-cells. *See e.g.*, '087 application, at page 1, lines 5-10 and 20-24; at page 105, lines 23-35; and at page 152, lines 26-30. In light of the above-described characterization of TR13, the '087 application provides compositions and methods of enhancing and inhibiting apoptosis, and teaches how these compositions and methods may be useful in the treatment of specific diseases including, for example, HIV infection and AIDS. *See e.g.*, '087 application at page 5, lines 10-11 and 20-21; at page 109, lines 20-23; and at page 111, lines 9-23. The '087 application further teaches that the compositions useful in enhancing and inhibiting apoptosis can be readily identified using techniques well known to one of skill in the art, specifically it states that "TR13 functional receptor activity can be measured using the cell death assays performed essentially as previously described ... [n]uclei of cells transfected with TR13 will exhibit apoptotic morphology." *See*, '087 application at Page 47, lines 21-28. Accordingly, Applicants contend that the '087 application clearly sets forth specific and substantial utilities of TR13 of the invention, and that one of skill in the art, on being

apprised of the teachings of the '087 application, would have found these asserted utilities to be credible.

In the present application Applicants have provided experimental evidence that TR13 regulates apoptosis and cell survival, in support of the teachings of TR13 function and assertions of utility in the '087 application. Applicants have demonstrated that TR13 activity does indeed regulate cell survival, TR13 activity serving to reduce fibroblast survival in a manner and to an extent comparable to the combination of Fas and FasL. *See*, example 37 at pages 416-417, and Figure 12. Applicants have further demonstrated that TR13 specifically binds a TNF ligand (FasL) to cause apoptosis. See, example 34 at pages 404-405. Contrary to the Examiner's assertion, Applicants contend that these data merely serve to support assertions of the '087 application, and do not constitute newly introduced matter in the present application. Furthermore, Applicants note that this supportive evidence provided in the present application, dated after the applicants' earliest claimed priority date, "can be used to substantiate any doubts as to asserted utility since it pertains to the accuracy of a statement already in the specification." *See e.g.*, *In re Brana* 51 F.3d 1560, 1567 at n19 (Fed. Cir. 1995). Accordingly, the assertions of utility made in the '087 application, having been credible at the time of filing, and later having been demonstrated to be true, are sufficient to constitute a showing of utility as required under 35 U.S.C. § 101.

In light of the above comments, Applicants assert that the '087 application, as well as each subsequently filed parent application, does indeed meet the statutory requirements of 35 U.S.C. §§ 101 and 112. Therefore, each of these applications is rightfully available for benefit of priority under 35 U.S.C. § 119(e) to the present application. Accordingly,

the effective priority date of the present application should correctly be the filing date of U.S. Provisional Application No. 60/144,087, *i.e.*, July 16, 1999.

VI. Rejections under 35 U.S.C. § 102

a. The Examiner has rejected claims 1, 4, 7, 10, 13, 16, 19-21, 23, 29-30, 34-38, 64, 65, 68, 71, 74, 75, 77, 80, 83, 86-96, 98-105, 107, 109, 111, 113, 115, 117-124 and 126-130 under 35 U.S.C. § 102(b) as allegedly "being anticipated by Bruck et al., WO 00/58460, October 5, 2000." *See*, Paper No. 8, page 13.

Applicants respectfully traverse the rejection. As discussed above, the correct effective priority date of the present application is July 16, 1999. Therefore, the teachings of Bruck et al., being published as a reference on October 5, 2000, do not qualify as prior art against the present application under 35 U.S.C. § 102. Accordingly, Applicants respectfully request that the present rejection of claims 1, 4, 7, 10, 13, 16, 19-21, 23, 29-30, 34-38, 64, 65, 68, 71, 74, 75, 77, 80, 83, 86-96, 98-105, 107, 109, 111, 113, 115, 117-124 and 126-130 under 35 U.S.C. § 102(b) as being anticipated by the teachings of Bruck et al. be reconsidered and withdrawn.

b. The Examiner has rejected claims 21 and 23 under 35 U.S.C. § 102(b) as allegedly "being anticipated by Edwards et al., US Patent No 5,736,363, April 7, 1998." *See*, Paper No. 8, page 14.

More specifically the Examiner alleges that "Edwards et al. disclose a nucleic acid molecule (SEQ ID NO:9) that encodes a polypeptide (SEQ ID NO:10) comprising an amino acid sequence (amino acids 110-117 of SEQ ID NO:10) that is identical to amino acids 680-687 of SEQ ID NO:40 of the instant application. Since an epitope-bearing

peptide can comprise at least 7 amino acids, the nucleic acid molecule encoding the polypeptide comprising the 8 amino acid portion of Edwards meets the limitations of the claims" *See*, Paper No.8, page 15. Applicants respectfully disagree and traverse the rejection. However, in the interest of expediting prosecution, Applicants have amended claim 21, and also dependent claim 23, to recite "of at least 9 amino acids" thereby mooting the present rejection.

Accordingly, Applicants respectfully request that the present rejection of claims 21 and 23 under 35 U.S.C. § 102(b) as being anticipated by the teachings of Edwards et al. be reconsidered and withdrawn.

c. The Examiner has rejected claims 1, 4, 7, 10, 13, 16, 19-21, 23, 28-30, 34-38 and 64-130 under 35 U.S.C. § 102(a) as allegedly "being anticipated by Ruben et al., WO 01/05834, January 25, 2001." *See*, Paper No. 8, page 15.

Applicants respectfully traverse the rejection. As discussed above, the correct effective priority date of the present application is July 16, 1999. Therefore, the teachings of Ruben et al., being published as a reference on January 25, 2001, do not qualify as prior art against the present application under 35 U.S.C. § 102. Accordingly, Applicants respectfully request that the present rejection of claims 1, 4, 7, 10, 13, 16, 19-21, 23, 28-30, 34-38 and 64-130 under 35 U.S.C. § 102(a) as being anticipated by the teachings of Ruben et al. be reconsidered and withdrawn.

VII. Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 97 and 125 under 35 U.S.C. § 103(a) as allegedly "being unpatentable over Bruck et al., WO 00/58460, October 5, 2000, in view of Fleer et al., PN 5,876,969." *See*, Paper No. 8, page 17.

Applicants respectfully traverse the rejection. As discussed above, the correct effective priority date of the present application is July 16, 1999. Therefore, the teachings of Bruck et al., being published as a reference on October 5, 2000, do not qualify as prior art against the present application under 35 U.S.C. § 103. Accordingly, Applicants respectfully request that the present rejection of claims 97 and 125 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Conclusion

Applicants respectfully request that the above-made remarks be entered and made of record in the file history of the instant application.

In view of the foregoing remarks, applicants believe that this application is now in condition for allowance. An early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by applicant would expedite the examination of this application.

Finally, if there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Dated: August 19, 2003

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Enclosures
KKH/LJH/BM/lcc